

AMENDMENTS TO THE CLAIMS

1. **(Currently amended)** A sample processing tubule, comprising:
a proximal end having an opening through which a sample is introducible;
a distal end; and
at least a first segment containing a solid substrate, a second segment distal to the
first segment and containing a wash reagent, and a third segment distal to
the second segment and containing at least one of an amplification reagent
and a detection reagent, three segments, each of which segments is:
defined by the tubule;
fluidly isolated, at least in part by a breakable seal;
so expandable as to receive a volume of fluid expelled from another
segment; and
so compressible as to contain substantially no fluid when so compressed;
~~and each of which contains at least one reagent.~~
2. (Original) The tubule of claim 1, wherein at least a portion of the tubule is transparent.
3. (Original) The tubule of claim 1, further comprising at least one pressure gate in fluid communication with at least one segment.
4. (Original) The tubule of claim 1, further comprising at least one filter in the tubule.

5. **(Currently amended)** The tubule of claim 1, wherein the tubule comprises at least one of ~~the reagents includes~~ a substance capable of specific binding to a preselected component of a sample when the sample is added to the tubule.
6. (Original) The tubule of claim 5, wherein the preselected component is nucleic acid.
7. (Original) The tubule of claim 6, wherein the substance capable of specific binding to nucleic acid includes at least one of an antibody, nucleic acid, peptide nucleic acid, phosphothioate nucleic acid, silica coated surface, electrostatically charged surface, and enzyme.
8. (Original) The tubule of claim 7, wherein the substance capable of specific binding to nucleic acid has a preselected amino acid or base sequence.
9. (Original) The tubule of claim 5, wherein the substance comprises at least one of a receptor, a ligand, an antibody, an antigen, a nucleic acid probe, a peptide nucleic acid probe, a phosphothioate nucleic acid probe, a bacteriophage, silica, and an electrostatic charged surface.
10. (Original) The tubule of claim 5, wherein the substance is capable of specific binding to a preselected component of at least one of bacteria, virus, parasite, cells, nucleic acid, and spores.
11. (Withdrawn) The tubule of claim 10, wherein the substance is capable of specific binding to a preselected component of at least one of *Yersinia pestis*, *Francisella tularensis*, *Listeria monocytogenes*, *Bacillus anthracis*, *Escherichia coli*, *Salmonella enteritidis*, *Campylobacter pylori*, *Campylobacter jejuni* *Clostridium*

perfringens, *Staphylococcus aureus*, *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitides*, *Vibrio cholerae*, *Mycobacterium tuberculosis*, and *Mycobacterium leprae*.

12. (Withdrawn) The tubule of claim 10, wherein the substance is capable of specific binding to a preselected component of at least one of human immunodeficiency virus 1, human immunodeficiency virus 2, influenza virus, yellow fever virus, dengue virus, hepatitis B virus, hepatitis C virus, cytomegalovirus, Epstein Barr virus, West Nile virus, hantavirus, and small pox.
13. (Withdrawn) The tubule of claim 10, wherein the substance is capable of specific binding to a preselected component of at least one of *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*, *Leishmania tropica*, *Leishmania donovani*, *Leishmania infantum*, *Leishmania major*, *Leishmania mexicana*, *Leishmania chagasi*, *Leishmania brasiliensis*, and *Leishmania amazoniensis*.
14. (**Currently amended**) The tubule of claim 5, wherein the substance is coupled to a the solid substrate.
15. (Original) The tubule of claim 14, wherein the substance forms a coating on the solid substrate.
16. (Original) The tubule of claim 14, wherein the solid substrate comprises at least one of beads, a pad, a filter, a sheet, an electrostatic surface, and a portion of a tubule wall surface.

17. (Original) The tubule of claim 14, wherein the substrate comprises at least one of silica beads, magnetic beads, silica magnetic beads, glass beads, nitrocellulose colloid beads, and magnetized nitrocellulose colloid beads.
18. (Original) The tubule of claim 14, wherein the substance comprises silica, and the substrate comprises a filter or a sheet.
19. (Withdrawn) The tubule of claim 14, wherein the substrate comprises a pad formed at least in part from an absorbent material comprising at least one of paper, film, filter, foam, mesh, and fiber matrix.
20. (Withdrawn) The tubule of claim 14, wherein the substrate is coupled to a tubule wall.
21. **(Withdrawn and currently amended)** The tubule of claim 1, ~~further comprising a substrate,~~ wherein the substrate comprises a pad formed at least in part from an absorbent material comprising at least one of paper, film, filter, foam, mesh, and fiber matrix.
22. (Canceled) ~~The tubule of claim 1, further comprising an open end for introducing a sample into the tubule.~~
23. **(Currently amended)** The tubule of claim 1, ~~[[22,]]~~ further comprising a cap for closing the open end.
24. (Original) The tubule of claim 23, wherein the cap comprises a sample collection device including at least one of a swab, a stick, a scoop, an inoculation loop, a forceps, a dropper, a capillary tube, and a syringe.

25. (Original) The tubule of claim 24, wherein the sample collection device is so disposed in or on the cap as to transfer a sample from the device to the tubule when the cap is positioned in relation to the tubule to close the open end of the tubule.
26. (Original) The tubule of claim 23, wherein the cap defines a cavity containing a chamber in fluid communication with the tubule.
27. (Original) The tubule of claim 23, wherein the cap comprises a member defining an expandable chamber in the cap.
28. (Original) The tubule of claim 27, wherein a cap wall defines a vent.
29. (Original) The tubule of claim 1, further comprising a frame to which the tubule is mounted.
30. **(Currently amended)** The tubule of claim 29, wherein the frame comprises an interface, the interface receiving the proximal ~~an open~~-end of the tubule.
31. **(Currently amended)** The tubule of claim 30, wherein the interface also receives a cap, thereby sealing the proximal ~~open~~-end of the tubule.
32. **(Currently amended)** The tubule of claim 1, ~~wherein at least one reagent comprises further comprising at least one of a diluent~~dilution buffer, suspension reagent~~buffer~~, substrate, lysis reagent, neutralization reagent, ~~wash buffer~~, elution reagent, proteolytic reagent, glycosylase, nucleic acid, nuclease, ligase, alcohol, reverse transcription reagent, and germination reagent, ~~and an amplification reagent~~.
33. **(Withdrawn and currently amended)** The tubule of claim 32~~[[1]]~~, wherein at ~~least one reagent comprises an~~ the tubule comprises an elution reagent ~~elution~~

~~buffer~~ that includes at least one of Tris buffer, water, and buffer suitable for polymerase chain reaction.

34. **(Withdrawn and currently amended)** The tubule of claim 32[[1]], wherein ~~at least one reagent comprises a~~ the tubule comprises a lysis reagent that includes at least one of a guanidinium salt, a chaotropic salt, a red blood cell lysis reagent, a detergent, a chelator, a spore germination reagent, sodium hydroxide, proteinase K, DNase inhibitor, RNase, RNase inhibitor, anticoagulant, coagulant, a protease, a germinant solution, and a surfactant.
35. **(Withdrawn and currently amended)** The tubule of claim 32[[1]], wherein ~~at least one reagent comprises~~ the tubule comprises a germination reagent including heart brain infusion medium and at least one of L-alanine, inosine, L-phenylalanine, L-Serine and L- proline.
36. (Original) The tubule of claim 1, wherein at least one breakable seal is a peelable seal.
37. (Original) The tubule of claim 1, wherein each breakable seal is a peelable seal.

Claims 38-43 (Canceled)

44. (Original) The tubule of claim 1, wherein the segments form a substantially linear array.
45. (Original) The tubule of claim 1, wherein the segments form a contiguous array.
46. (Canceled)
47. **(Currently amended)** A sample processing tubule, comprising:
a substantially linear array of contiguous segments, each of which is:

defined by the tubule;

fluidly isolated, at least in part by a breakable seal;

so expandable as to receive a volume of fluid expelled from another
segment; and

so compressible as to contain substantially no fluid when so compressed;

wherein:

a segment contains at least one of a lysis reagent and a ~~diluent~~dilution
~~buffer~~;

a segment contains at least a nucleic acid binding reagent;

a segment contains at least a wash ~~reagent~~buffer;

a segment contains at least a nucleic acid eluting reagent; and

a segment contains at least nucleic acid amplification reagents.

48. **(Withdrawn and currently amended)** A method of processing a sample,

comprising:

introducing a sample into a tubule discretized by breakable seals into a plurality of

fluidly isolated segments, wherein the tubule has a proximal end for
receiving waste and a distal end for conducting an assay;

incubating the sample in a segment of the tubule with a ~~solid~~substrate ~~to~~stance
~~capable of specific binding to~~ a preselected component of the sample;

removing waste from the preselected component by clamping the tubule distally of
the segment containing the preselected component and compressing that
segment; and

releasing a wash reagent to mix with the preselected component from a fluidly isolated adjacent distal segment by compressing at least one of the segment containing the preselected component and a segment containing the wash reagent distal of that segment, thereby opening a breakable seal and either propelling the wash reagent into the segment containing the preselected component or propelling the preselected component into the segment containing the wash reagent, and

releasing at least one of an amplification reagent and a detection reagent to mix with the preselected component from a fluidly isolated adjacent distal segment by compressing at least one of the segment containing the preselected component and a segment containing the at least one of an amplification reagent and a detection reagent distal of that segment, thereby opening a breakable seal and either propelling the at least one of an amplification reagent and a detection reagent into the segment containing the preselected component or propelling the preselected component into the segment containing the at least one of an amplification reagent and a detection reagent.

49. **(Withdrawn and currently amended)** The method of claim 48, further comprising capturing the substrate~~substance~~.
50. **(Withdrawn and currently amended)** The method of claim 48, wherein the ~~substance~~-substrate comprises at least one of a sheet, a portion of the tubule wall, a pad, a filter, or magnetic beads.

51. **(Withdrawn and currently amended)** The method of claim ~~48~~50, wherein a the substance capable of specific binding to a preselected component of a sample is coupled to the substrate, ~~at least one of a sheet, a portion of the tubule wall, a pad, a filter, or magnetic beads.~~
52. **(Withdrawn and currently amended)** The method of claim 48, wherein the ~~substance is coupled to~~ substrate comprises magnetic beads, and the method further comprises applying a magnetic field.
53. (Withdrawn) The method of claim 48, wherein removing further comprises sequentially compressing segments containing the waste in distal-to-proximal order.
54. (Withdrawn) The method of claim 48, further comprising reconstituting a dry reagent by clamping the tubule adjacent to a segment containing a reconstitution fluid and compressing that segment, thereby opening a breakable seal and propelling a reconstitution fluid into an adjacent segment containing the dry reagent.
55. (Withdrawn) The method of claim 48, further comprising forming a thin-layer flow channel in a segment by so compressing the segment as to leave a gap.
56. (Withdrawn) The method of claim 48, further comprising mixing a quantity of fluid by alternately compressing adjoining segments containing the quantity of fluid.
57. (Withdrawn) The method of claim 48, further comprising agitating a quantity of fluid in a segment by repeatedly compressing and relaxing the segment.

58. (Withdrawn) The method of claim 48, further comprising urging the sample through a filter.
59. (Withdrawn) The method of claim 48, wherein the preselected component comprises a nucleic acid, and the method further comprises amplifying the nucleic acid by at least one of polymerase chain reaction, reverse transcription polymerase chain reaction, rolling circle amplification, ligase chain reaction, nucleic acid based amplification, transcription mediated amplification, and strand displacement amplification reaction.
60. (Withdrawn) The method of claim 48, wherein the preselected component comprises a ribonucleic acid, and the method further comprises synthesizing deoxyribonucleic acid by reverse transcription.
61. (Withdrawn) The method of claim 60, further comprising amplifying the synthesized deoxyribonucleic acid by at least one of polymerase chain reaction, rolling circle amplification, ligase chain reaction, nucleic acid based amplification, transcription mediated amplification, and strand displacement amplification reaction.
62. (Withdrawn) The method of claim 48, wherein the preselected component comprises a ribonucleic acid, the method further comprises synthesizing and amplifying deoxyribonucleic acid by reverse transcription–polymerase chain reaction.
63. (Withdrawn) The method of claim 48, wherein the preselected component comprises a nucleic acid, and the method further comprises circularizing a single-

- stranded padlock probe with T4 DNA ligase, selecting single stranded circular padlock probes with exonuclease I and exonuclease III, linearizing the single stranded circular padlock probes and amplifying the linearized padlock probes.
64. (Withdrawn) The method of claim 48, further comprising circularizing a single-stranded padlock probe with T4 DNA ligase, and amplifying the single stranded circular DNA probes with rolling circle amplification.
65. (Withdrawn) The method of claim 48, further comprising detecting the amplification product.
66. (Withdrawn) The method of claim 65, wherein detecting comprises measuring light emission from a dye coupled to the amplification product.
67. (Withdrawn) The method of claim 48, further comprising obtaining the sample, wherein the sample comprises at least one of cells, bacteria, spores, virus, microbial organisms, buccal cells, cervical cells, biopsy tissues, stool, biological fluid, allantoic fluid, amniotic fluid, ascitic fluid, bile, bile acids, bile salts, bile pigments, blood, blood plasma, blood serum, cerebrospinal fluid, chorionic fluid, colostrum, digestive juice, gastric juice, intestinal juice, pancreatic juice, exudate, hemolymph, lochia, lymph, chyle, milk, mucus, pericardial fluid, peritoneal fluid, perspiration, pleural fluid, saliva, sebum, semen, seminal fluid, sputum, synovial fluid, tear, transudate, urine, vaginal fluid, soil, and environment water.
68. (Withdrawn) The method of claim 48, wherein the sample comprises spores and the method further comprises incubating the sample with a germination solution, whereby the spores are induced to germinate.

69. (Withdrawn) The method of claim 48, further comprising grinding the sample.
70. (Withdrawn) The method of claim 48, further comprising adjusting the volume of a fluid by compressing a segment to set a specific volume within the tubule segment and closing a clamp to define the volume within the segment and isolate excess volume in an adjacent segment.
71. (Withdrawn) The method of claim 48, further comprising removing an air bubble by agitating a segment containing a liquid and adjusting a volume of the segment to section the air to an adjacent segment.
72. (Withdrawn) The method of claim 48, further comprising preferentially opening a first breakable seal by physically protecting a second breakable seal region with an actuator or a clamp to prevent the second breakable seal from breaking while compressing the segment to break the first breakable seal.
73. (Withdrawn) The method of claim 48, further comprising preferentially breaking a breakable seal, by compressing a segment adjacent to the first breakable seal such that the first breakable seal is broken by the pressure created in the adjacent segment, thereby so lowering the pressure in the combined segment as to be insufficient to break a second breakable seal located adjacent to the uncompressed segment.
74. (Withdrawn) The method of claim 48, further comprising eluting the sample by opening a breakable seal separating a segment containing an elution reagent from the sample.

75. (Withdrawn) The method of claim 48, further comprising lysing the sample by opening a breakable seal separating a segment containing a lysis reagent from the sample.
76. (Previously presented) The tubule of claim 1, wherein at least one of the reagents is in a dry format.
77. (Previously presented) The tubule of claim 1, wherein the breakable seal is so formed that bursting of the breakable seal leaves an inner tubule surface that is substantially free of obstructions to fluid flow.
78. (Previously presented) The tubule of claim 77, wherein the segments form a substantially linear array.
79. (Previously presented) The tubule of claim 78, wherein the segments form a contiguous array.
80. (Previously presented) The tubule of claim 1, wherein the segments form a contiguous and substantially linear array.

Claims 81-84. (Canceled)

85. (**New**) The tubule of claim 1, further comprising at least a fourth segment that (a) is distal to the second segment and (b) contains at least one of an elution reagent, second wash reagent, lysis reagent, reverse transcription reagent, a nucleic acid, a nuclease, and glycosylase.
86. (**New**) The tubule of claim 1, further comprising at least a fourth segment that (a) is proximal to the first segment and (b) contains at least one of a germination reagent, suspension reagent, lysis reagent, neutralization reagent, diluent, second wash

- reagent, elution reagent, nucleic acid, proteolytic reagent, and a substance capable of specific binding to a preselected component of a sample.
87. **(New)** The tubule of claim 1, further comprising at least a fourth segment that (a) is distal to the third segment and (b) contains at least one of a second amplification reagent, a nuclease, a second detection reagent, and a glycosylase.
88. **(New)** The tubule of claim 1, further comprising at least a fourth segment that (a) is distal to the first segment and (b) contains at least one of a diluent, suspension reagent, nucleic acid, lysis reagent, second wash reagent, and alcohol.
89. **(New)** The tubule of claim 1, further comprising:
a fourth segment that (a) is proximal to the first segment and (b) contains at least one of a lysis reagent and a diluent; and
a fifth segment that (a) is distal to the second segment, (b) proximal to the third segment, and (c) contains an elution reagent.
90. **(New)** The tubule of claim 1, wherein the amplification reagent in the third segment comprises at least one of a nucleic acid polymerase and nucleotide triphosphates.
91. **(New)** The tubule of claim 1, wherein the solid substrate in the first segment specifically binds nucleic acid.